fMRI-based Neurofeedback of the basal ganglia in Parkinson*s disease

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Primary Objective: Assess the effect of mental imagery with fMRI-neurofeedback-based upregulation of the putamen on motor symptoms of PD Secondary Objective(s): -Assess changes in whole brain activation patterns over the course of the NF training -...

Ethical review	Approved WMO
Status	Pending
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON57162

Source
ToetsingOnline

Brief title
BG-PD fMRI Neurofeedback

Condition

- Movement disorders (incl parkinsonism)

Synonym
Shaking palsy

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Neurofeedback, Parkinsons, Real-time, Self-regulation

Outcome measures

Primary outcome

We will compare changes in the MDS-UPDRS part III: Motor Examination score pre vs. post treatment between the two groups with the appropriate parametric (if assumptions for parametric tests are met) or non-parametric test.

Secondary outcome

-Changes in whole brain activation patterns over the course of the NF training as measured from the fMRI during the localiser task and subsequent NF runs

-Effect of NF training on non-motor symptoms as assessed by the MDS-UPDRS part I: Non-Motor Aspects of Experiences of Daily Living at 1-month follow-up.

-Effect of NF training on motor symptoms in everyday situations assessed by the MDS-UPDRS part II: Motor Aspects of Experiences of Daily Living and part IV: Motor Complications at 1-month follow-up.

-Correlations between NF success and additional behavioral parameters such as finger tapping speed measured by the Distal Finger Tapping task (Akram et al., 2022).

-Exploration of potential predictors of NF success by machine-learning based

analysis of the fMRI and clinical data

Study description

Background summary

Parkinson*s disease (PD) is associated with progressive neurodegeneration of dopaminergic neurons of the substantia nigra. It is characterized by both motor and non-motor system manifestations. Dopamine replacement therapy or dopaminergic medication are the key therapeutic strategies, but deep brain stimulation (DBS) is increasingly being used in cases where drug response is/ has become insufficient or hampered by unacceptable side effects (Hartmann et al., 2019; Lee et al., 2018).

Neurofeedback (NF) entails training of self-regulation of brain regions or networks via mental imagery and real-time feedback of neural signals, for example obtained by functional MRI (fMRI). NF enables patients to develop personal strategies that are most effective in self-regulating brain areas and networks. Thereby, it can provide an individually tailored intervention (Linden, 2014). NF is a highly sustainable form of non-invasive neuromodulation because, once learnt, the self-regulation strategies can in principle be applied by patients whenever needed to overcome disease symptomology.

NF can be used to train patients to change their brain activity in different directions, or to modulate patterns of co-activation between regions. Mental imagery of moving one*s own body (also called kinaesthetic imagery) can potentially be used to improve motor functions and neuroplasticity in PD (Sarasso et al., 2023). Kinaesthetic imagery is also a suitable strategy for increasing activation in the brain*s motor network, and motor imagery training can be reinforced through combination with NF. A NF paradigm involving upregulation training of motor areas through kinaesthetic imagery thus has good plausibility for PD. The PI*s group has shown proof-of-concept of such an fMRI-NF training (targeting the supplementary motor area, SMA) in PD (Subramanian et al., 2011, 2016) and is currently conducting a feasibility study of fMRI-NF targeting the putamen in 12 PD patients (METC study number NL82024.068.22 / METC22-052). FMRI-NF targeting of the putamen has become available in a medical product, the software TurboBrainVoyager MED (TBV-MED), and the aim of the current investigator-initiated study is to investigate the effects of putamen upregulation training on motor function in PD.

Study objective

Primary Objective:

Assess the effect of mental imagery with fMRI-neurofeedback-based upregulation of the putamen on motor symptoms of PD

Secondary Objective(s):

-Assess changes in whole brain activation patterns over the course of the NF training

-Assess effects on non-motor symptoms

-Assess correlations between NF success and additional behavioral parameters

-Explore potential predictors of NF success

Study design

This is a randomized controlled trial for the application of fMRI-neurofeedback targeting subcortical regions of the motor control network during mental imagery in patients with PD. The primary outcome measure will be the post-interventional change in the MDS-UPDRS (Unified Parkinson's Disease Rating Scale) motor scale widely used in the clinic to assess the motor symptoms of PD.

Following initial contact with patients through one of the collaborating clinical teams, a suitably qualified member of the study team or patient representatives will provide patients with information about the study. The patients can then contact the study team to schedule a date for the screening session (at the earliest 7 days after participants received the study information). At the start of the screening session consent will be taken. The patients will be randomly allocated into either the experimental or the control group. In both groups, patients will perform an approximately 10 week-long mental training including motor imagery. During this period, patients in the experimental group will be subjected to four weekly MRI sessions where they will learn to upregulate the activity of the putamen during motor imagery via fMRI neurofeedback. In the control group, motor imagery is also performed during the MRI sessions, but no feedback is provided to the patient. After the last fMRI session and at 1 month follow-up, a post-training assessment of the symptoms will be conducted. The study will test the hypothesis that the experimental group will experience a larger improvement in the MDS-UPDRS part III: Motor Examination scale after the last MRI session compared to the control group.

Intervention

The patients will be randomly allocated into either the experimental or the

control group. Both groups will be asked to take part in a total of four fMRI sessions. The first MRI measurement session will be scheduled approximately one week after screening. This provides some further delay for the patients to be able to reconsider their agreement and withdraw their consent before the actual start of the intervention if desired. Both groups will then be invited for another three fMRI measurement sessions in approximately weekly intervals. After the last NF session, a post-training assessment of clinical measures will be conducted. The intervention will thus be concluded after approximately 5-6 weeks. One further follow-up assessment (1 month after the last MRI-session) will conclude the trial. Therefore, the total on-site visits in the trial will be six; one for the initial screening and baseline assessment, four for the MRI measurements and one meeting for the follow-up assessment. All patients of this group will be asked to practice the motor imagery they have been doing in the scanner also on the days between the fMRI-sessions and to keep a diary of this practice (suggested time minimally 10 minutes per day). A diary template will be offered (see appendix F2 Patient Diaries).

Study burden and risks

No risks or harm were identified in relation to the neurofeedback procedure, no risk control measures were defined and implemented that are specific to the neurofeedback treatment. However, we have implemented general risk management procedures as appropriate for this population, including accessibility of clinical professionals if needed. There are no known safety issues arising from fMRI-based neurofeedback over and above general MRI safety requirements (for which strict guidelines implemented at Scannexus will be followed).

The overall time commitment (excluding travel) will be approximately 11 hours. Patients will be compensated for their time (10¤ / hour) and travel costs. Previous work (Subramanian et al., 2011; 2016) has shown that fMRI-NF may have a clinically relevant effect (improvement of 5 points on the MDS-UPDRS part III: Motor Examination). The participants stand to potentially benefit from therapeutic effects due to the neurofeedback intervention. Non-clinical benefits include creation of a feeling of control as well as learning about non-invasive methodologies for self-regulation that the participants can implement outside the scanner at a later time.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Diagnosis of Parkinson*s disease

-Disease stage 1-3 according to the Hoehn and Yahr Scale

-Age: 18 years or more

Exclusion criteria

-Exclusion criteria for MRI (e.g., cardiac pacemaker, certain metallic implants)

-History of psychotic disorder, bipolar disorder, or psychotic depression

-Current use of illegal drugs (any in the last four weeks)

-Current excessive alcohol consumption that interferes with daily functioning

-A score on the Montreal Cognitive Assessment (MoCA) below 24/30.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2024
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Generic name:	Turbo-BrainVoyager MED PD (TBV MED PD)
Registration:	No

Ethics review

Approved WMO

Date:	09-12-2024
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	Applied for NCT, result pending
CCMO	NL86308.068.24